Prevention of neonatal pneumonia and sepsis via maternal immunisation

Published Online
November 12, 2014
http://dx.doi.org/10.1016/S2214-109X(14)70317-1

Pneumonia is the leading killer of children younger than 5 years, and the greatest risk of mortality from pneumonia in childhood is in the neonatal period.[1] Substantial reductions in childhood pneumonia deaths have been hindered by a lack of progress in addressing neonatal mortality. Deaths in the neonatal period constitute 41·6% of the 6·3 million children who die annually before their fifth birthday.[2] In 2010, there were an estimated 1·7 million cases of neonatal sepsis and 510 000 cases of neonatal pneumonia.[3] On Nov 12, World Pneumonia Day, we focus on prevention of pneumonia in these youngest and most susceptible victims.

Early-onset neonatal pneumonia is mostly acquired from the mother during labour or delivery, and commonly presents with respiratory distress beginning at, or soon after, birth. Because signs of pneumonia are non-specific in neonates, any newborn infant with sudden onset of respiratory distress or other signs of illness should be assessed for pneumonia and sepsis. Successful treatment depends on the pathogen, early recognition of the infection, and prompt therapy before the development of irreversible injury. In resource-limited settings, however, timely diagnosis and treatment is often not possible and mortality is high.

Efforts to prevent neonatal pneumonia and sepsis have been few, despite being essential for reduction of this high mortality. Active immunisation is not always possible in neonates because of the immaturity of the neonatal immune system and the several weeks necessary for protective immunity to develop. Beyond herd protection of neonates through immunisation of older children with *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) conjugate vaccines, existing vaccine interventions during infancy have so far not substantially reduced neonatal mortality. Maternal immunisation is a viable approach for protection of young infants from the most common infectious causes of mortality, both by allowing sufficient protection through the passive placental transfer of maternal antibodies to the fetus and by enabling reduced mother-to-child transmission of infection. Safe and effective, maternal antenatal immunisation allows the neonate to acquire necessary pathogen-specific antibody concentrations to fight infections during a discrete but heightened period of susceptibility.[4]

For example, through sustained emphasis on improvement of vaccination coverage, the Maternal and Neonatal Tetanus Elimination Initiative has made substantial progress in the elimination of maternal and neonatal tetanus.[5] The H1N1 influenza pandemic in 2009 prompted new recommendations for routine maternal immunisation against influenza and pertussis in pregnant women in the USA and UK.[6] In response to an outbreak across England, a pertussis vaccination programme for pregnant women was introduced in 2012. It has been shown to have high vaccine effectiveness among infants.[7] In a small trial from Bangladesh, influenza vaccination of mothers in addition to pneumococcal conjugate or Hib vaccination of their infants was effective against respiratory illness during early infancy.[8] Furthermore, maternal influenza immunisation in a 2014 South African trial showed vaccine efficacy both among mothers infected with HIV and among uninfected mothers, and protection of HIV-uninfected infants.[9] Currently, influenza trials in Mali, Nepal, and South Africa are studying a wide range of benefits to the mother, fetus, and for the first 6 months of life, the neonate.

The opportunity to increase the coverage of influenza and pertussis immunisation in pregnant women in developing countries is substantial, but several challenges are clear. WHO recommends maternal pertussis vaccination as the most cost-effective strategy for reduction of neonatal pertussis mortality in high-burden countries, but obstacles remain. These include diagnostic challenges, under-reporting, and a paucity of data on incidence of neonatal pertussis.[10] Furthermore, the acellular pertussis vaccines available at present are expensive. Development of an effective low-cost vaccine is essential for adoption in low-income countries.

There is also scope to develop new maternal vaccines to protect infants. Group B streptococci (GBS) and respiratory syncytial virus (RSV) infections are serious and frequent causes of neonatal morbidity and mortality, and offer important potential opportunities for maternal immunisation.[11] One in four women

carry GBS vaginally.[12] At increased risk of infection and mortality, up to 3% of infants with very low birthweights become infected, with mortality rates of up to 30%, even with immediate antibiotic treatment. Maternal GBS vaccination would be cost-effective.[13,14] The safety and immunogenicity of a maternal GBS candidate vaccine is under evaluation. First lifetime RSV infections are responsible for up to 22% of severe lower respiratory tract infections in children younger than 5 years. They occur at a very early age, in a seasonal pattern, and lead to bacterial coinfections in about a third of patients.[15] GBS and RSV vaccines are crucial to reduction of neonatal mortality, and maternal immunisation shows potential to achieve improved protection of the neonate.

As shown by tetanus, influenza, and pertussis vaccination during pregnancy, maternal immunisation is a safe and effective approach for prevention of infection in neonates, and could be a promising strategy to address neonatal pneumonia and sepsis.

*Amy Sarah Ginsburg, Ajoke Sobanjo-ter Meulen, Keith P Klugman

PATH, PO Box 900922, Seattle, WA 98109, USA (ASG); Bill & Melinda Gates Foundation, Seattle, WA, USA (AS-tM, KPK)

aginsburg@path.org

We declare no competing interests.

1 Nissen MD. Congenital and neonatal pneumonia. *Paediatr Respir Rev* 2007; **8:** 195–203.

2 Wang H, Liddell CA, Coates MM, et al. Global, regional, and national levels of neonatal, infant, and under-5 mortality during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014; **384:** 957–79.

3 Seale AC, Blencowe H, Zaidi A, et al, for the Neonatal Infections Estimation Team. Neonatal severe bacterial infection impairment estimates in South Asia, sub-Saharan Africa, and Latin America for 2010. *Pediatr Res* 2013; **74** (suppl 1)**:** 73–85.

4 Glezen WP, Alpers M. Maternal immunization. *Clin Infect Dis* 1999; **28:** 219–24.

5 Thwaites CL, Beeching NJ, Newton CR. Maternal and neonatal tetanus. *Lancet* 2014; published online Aug 19. http://dx.doi.org/10.1016/S0140-6736(14)60236-1.

6 Lindsey B, Kampmann B, Jones C. Maternal immunization as a strategy to decrease susceptibility to infection in newborn infants. *Curr Opin Infect Dis* 2013; **26:** 248–53.

7 Amirthalingam G, Andrews N, Campbell H, et al. Effectiveness of maternal pertussis vaccination in England: an observational study. *Lancet* 2014; published online July 15. http://dx.doi.org/10.1016/S0140-6736(14)60686-3.

8 Omer SB, Zaman K, Roy E, et al. Combined effects of antenatal receipt of influenza vaccine by mothers and pneumococcal conjugate vaccine receipt by infants: results from a randomized, blinded, controlled trial. *J Infect Dis* 2013; **207:** 1144–47.

9 Madhi SA, Cutland CL, Kuwanda L, et al, for the Maternal Flu Trial (Matflu) Team. Influenza vaccination of pregnant women and protection of their infants. *N Engl J Med* 2014; **371:** 918–31.

10 World Health Organisation. *Wkly Epidemiol Rec* 2014; **89:** 221–36.

11 Shaw CA, Ciarlet M, Cooper BW, et al. The path to an RSV vaccine. *Curr Opin Virol* 2013; **3:** 332–42.

12 Le Doare K, Heath PT. An overview of global GBS epidemiology. *Vaccine* 2013; **31** (suppl 4)**:** D7–12.

13 Kim SY, Russell LB, Park J. Cost-effectiveness of a potential group B streptococcal vaccine program for pregnant women in South Africa. *Vaccine* 2014; **32:** 1954–63.

14 Oster G, Edelsberg J, Hennegan K, et al. Prevention of group B streptococcal disease in the first 3 months of life: would routine maternal immunization during pregnancy be cost-effective? *Vaccine* 2014; **32:** 4778–85.

15 Weigl JA. RSV–a substantial slice of the airway disease burden and the way to a vaccine. *Paediatr Int Child Health* 2012; **32** (suppl 2)**:** S9–15.